Geriatric Pharmacotherapy: Optimisation Through Integrated Approach in the Hospital Setting

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Abstract Since older patients are more vulnerable to adverse drug-related events, there is a need to ensure appropriate prescribing in these patients in order to prevent misuse, overuse and underuse of drugs. Different tools and strategies have been developed to reduce inappropriate prescribing; the available measures can be divided into medication assessment tools, and specific interventions to reduce inappropriate prescribing. Implicit criteria of inappropriate prescribing focus on appropriate dosing, search for drug-drug interactions, and increase adherence. Explicit criteria are consensus-based standards focusing on drugs and diseases and include lists of drugs to avoid in general or lists combining drugs with clinical data. These criteria take into consideration differences between patients, and stand for a medication review, by using a systematic approach. Different types of interventions exist in order to reduce inappropriate prescribing in older patients, such as: educational interventions, computerized decision support systems, pharmacist-based interventions, and geriatric assessment. The effects of these interventions have been studied, sometimes in a multifaceted approach combining different techniques, and all types seem to have positive effects on appropriateness of prescribing. Interdisciplinary teamwork within the integrative pharmaceutical care is important for improving of outcomes and safety of drug therapy. The pharmaceutical care process consists of four steps, which are cyclic for an individual patient. These steps are pharmaceutical anamnesis, medication review, design and follow-up of a pharmaceutical care plan. A standardized approach is necessary for the adequate detection and evaluation of drug-related problems. Furthermore, it is clear that drug therapy should be reviewed in-depth, by having full access to medical records, laboratory values and nursing notes. Although clinical pharmacists perform the

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pharmaceutical care process to manage the patient's drug therapy in every day clinical practice, the physician takes the ultimate responsibility for the care of the patient in close collaboration with nurses.

Keywords Geriatric pharmacotherapy · Optimization · Integrated approach

Introduction

Older individuals are more susceptible to adverse drug reactions (ADRs), which can occur while they are hospitalized due to multiple comorbidities, the progression of these conditions, the complexity of the therapeutic regimen or even drug-drug interactions, but can also be the primary cause of hospitalization [1, 2]. While the percentages of ADRs for all hospitalized patients vary between 2.4 and 10.9 % [3, 4], the incidence of ADRs is higher in older people as they take far more drugs than younger individuals, the higher frequency being a common risk factor for the development of ADRs. Therefore, it is of utmost importance that physicians to understand the therapeutic schedule prescribed, the drugs being used by the patients and the drug effects being experienced by the patients being submitted to the hospital. However, obtaining accurate figures for older people is complicated by the voluntary ADR reporting system in which it is known that under-counting is an issue [5, 6]. Consequently, to avoid under-reporting, thought should be given to combining information from physicians and nurses with data obtained directly from the patient, perhaps via direct interview while staff members are making ward rounds.

Although as a cause of hospital admissions, the percentage related to drug issues varies considerably from 4 to 30 %, the majority are related to ADRs which are considered avoidable in 50–97 % of the cases [7–9]. Moreover, while only 5.6 % of the 13,000 unplanned hospital admissions analyzed in the prospective Hospital Admissions Related to Medications study (HARM) were classified as drug-related, the mean age of this population was significantly higher compared to overall mean population age, suggesting drug-related hospital admissions were more common in older individuals [10].

It is also important to separate out the general factors responsible for the high incidence of drug-related problems in older people [11–17], versus other factors that further modulate the rate of ADRs in the hospital setting. In regard to the former, it is common for older people to have many diseases at the same time that may be treated with a variety of different drugs, which obviously increases the complexity of the drug therapy for patients as well as the risk for adverse drug events, including undesirable drug-drug interactions. Second, physiological and biopharmaceutical changes in older people may be responsible for different pharmacokinetic and pharmacodynamic profile of drug products contributing to unanticipated ADRs due to the lack of focus on the older and complex patient populations in the clinical trial program during the development and marketing of

the drug product. Another important consideration is the fact that, in an age in which many older patients see several specialists in addition to and independently from their primary care physicians, lack of coordination can increase the difficulty to evaluate the overall medication schedule of the patient. This lack of coordination can relate to indications for drug prescription, courses of therapies, the monitoring of ADRs, and assessing drug effectiveness for the different medical problems for which they were prescribed. Last but not least, older persons are also often challenged cognitively and physically to handle their medications (for example, removing tablets or capsules from blister packs, or using inhalation devices appropriately including the required inhalation techniques), which can results in unsatisfactory compliance or inappropriate drug use and therapeutic outcomes. Finally, it must be remembered that while older people are typically prescribed the same drugs as younger adults often based on a "single disease" examination and treatment view, many more drugs are being prescribed simultaneously (polypharmacy) with the possibility that some of the drugs may not exhibit the expected and desired efficacy and safety profile [8–10].

In the hospital setting, older patients are often placed into acute geriatric wards. But, despite good professional care that includes evidence-based pharmacotherapy, inappropriate drug prescription still continues to occur thus elevating the risk of ADRs [18–20]. The major reason is continuation of drug therapy initiated prior to hospitalization plus additional drug prescription based on the acute treatment plan. This practice gives rise to simultaneous administration of previously and newly prescribed drugs without complete evaluation as to which drugs are really required, should be continued, changed, temporarily or definitely stopped, as well as lacks the necessary follow-up of the therapeutic effects and side-effects.

Designing strategies to prevent drug-related problems (DRPs) in older people requires close attention to the associated factors in the hospital itself and incrementally must address the transition between settings: admission to other hospitals and discharge to the home or long-term care facilities. Consequently, admission to the acute geriatric wards of a hospital affords both an opportunity to identify patients at high risk for DRPs and evaluation of medication discrepancies that already exist without compounding them further [21, 22].

Identification of Older Patients at Risk for Developing Adverse Drug Reactions

As a matter of fact, staffing resources within hospitals are often limited particularly when it comes to groups of individuals who need more attention than the 'average' patient. Consequently, within the multistep paradigm of geriatric pharmacotherapy, the first critical step is identification of those older patients who are most at risk for developing ADRs. This requires a continuous training of clinicians, nurses, and pharmacists in recognizing ADRs, which in daily practice is unfortunately not

achieved to the extend needed. Often an ADR is diagnosed and judged as a part of a disease-related clinical symptom rather than a drug-related problem per se, which may lead to further drug prescribing to control the ADR symptoms. In addition, such ADRs are complicating the definition of the medical diagnosis and increasing the chance for more drug-drug interactions, which, in turn, increases the odds that more ADRs will occur in a phenomenon termed 'the prescribing cascade' [23]. Consequently, any differential diagnosis should *always* include the possibility that presenting symptoms may be caused in part or wholly by an ongoing ADR. If a high-risk patient can be identified at admission those patients will receive extra attention from physicians, nurses, and pharmacists in regard to existing and new medications that will benefit most which in turn will mitigate the resource problem —as well as lower the chance of avoidable ADR occurrences and prescription cascading.

Two approaches have been recently reported in the literature which identify older patients at high risk for developing ADRs, both of which are simple and efficient: the GerontoNet ADR risk score [24] and the Brighton Adverse Drug Reactions Risk (BADRI) Model [25].

The GerontoNet risk score comprises those variables associated with ADRs and includes: four or more comorbid conditions (1 point); heart failure (1 point); liver disease (liver function test results that are more than twice the upper limit of normal) (1 point); number of daily drugs (maximum 4 points for ≥8 drugs, 1 point for 5–8 drugs, 0 points ≤5 drugs); previous ADRs (2 points); and renal failure (estimated GFR <60 mL/min) (1 point). Within the score range of 0–10 points a cut-off point of 3–4 presents a balance between optimal sensitivity (68 %) and specificity (65 %) in classifying those patients most at risk for an ADR.

Although the GerontoNet ADR risk score is simple to use, not requiring any clinical tests or complex biological parameters to be calculated, and can easily classify patients according to risk, it still has limitations. For example, in an observation study comprising 513 acutely ill patients aged ≥65 years, the GerontoNet ADR risk score incorrectly classified 38 % of patients as low risk [26].

The alternative more recent approach to assess ADR risk is the BADRI model [25], which is based on five clinical parameters with equal weighting: >8 drugs, hyperlipidaemia, elevated white cell count, use of antidiabetic agents, and length of hospital stay (>12 days). The best trade-off was found at a cut-off score of 1, yielding a good sensitivity of 80 % but a poorer specificity of 55 %. A major disadvantage of the BADRI model is that it requires length of the hospital stay in its calculation, which means that the score will not be assessed until 12 days have elapsed from initial admission. Validation results from European centres for both approaches were similar, although the BADRI results reflect a higher patient age and included possible ADRs rather than just definite and probable ADRs that were used in construction of the GerontoNet ADR risk score. Thus, although a promising start in this field, this methodological assessment of risk patients for ADRs will require further refinement with the addition of other variables and perhaps reweighting of its applicability and usability in routine practice where assessment of ADRs and identification of risk patents will have the highest impact. In addition,

such approaches will gain better acceptability and implementation when the assessment tools for ADRs will become more accurate.

Strategies to Reduce Inappropriate Drug Prescribing in Older Patients

One obvious solution to reducing ADRs in older people in any kind of clinical setting is to create a framework in which inappropriate drug prescribing is prevented or at least diminished. Specific settings may require different sets and combinations of interventions, explicit approaches include pharmacist-driven interventions, educational interventions, and instruments to detect inappropriate prescribing in older people, computerized decision support systems and geriatric medical services interventions (Table 1).

Pharmacist-Driven Interventions

Traditionally, pharmacists just dispensed the drug products according to the prescriptions. However, in the last 20 years there has been a gradual evolution towards a patient-centred viewpoint in which pharmacists are taking increasing responsibility for the drug therapy and welfare of their patients. Applying their specific pharmaceutical expertise, clinical pharmacists contribute to the overall assurance for the patient's safety and effectiveness of the prescribed drugs [27]. This evolution stems in part from a cyclical process applied each time a patient is prescribed a new medication whereby the pharmacist will perform pharmaceutical anamnesis, medication review, design of an individualized pharmaceutical care plan, and follow-up of the plan [28].

This process is far from perfect in practice because it is assumed that someone—the primary treating physician in most cases—actually takes responsibility for working through the cycle elements based on available medical records, laboratory values and nursing notes. Because electronic health records are not universally available and certainly not linked between healthcare institutions, the available information may be incomplete or even inaccurate, leading to erroneous conclusions. Nevertheless, the first step is identification of all medications the patient is taking, along with dosages, frequency, and route of administration. The second step is to review the medications in the context of what is known about the patient medically in a structured manner to identify inappropriate drug prescriptions taking into account the patient's limitations that could lead to misuse, overuse, underuse, or medication errors. This process should lead to the identification of possible DRPs. Discussion with the patient and other physicians prescribing existing medications should then take place so that a medication management plan can be

Table 1 Advantages and limitations of approaches to lower inappropriate drug prescribing

Approach	Advantages	Limitations
Pharmacist-driven intervention	• Pharmacist has more in-depth knowledge about drug adverse effects that treating physician • Can educate other healthcare professionals	• Mixed/insufficient evidence for effect on health outcomes, health related quality of life and cost-effectiveness of care • Working outside of the multidisciplinary team often fails
Educational intervention	• Ongoing individualized, interactive, multidisciplinary, and multifaceted programs can be helpful	• Need to define what is required to assess adequacy for a given level of intervention • Mere dissemination of guidelines unlikely to be effective
Instruments to detect inappropriate prescribing in older people	• Implicit: comprehensive and systematic approach; includes operational definitions, clear instructions and examples; good as an educational tool • Explicit: relatively easy to remember and to detect; provide support to identify inappropriate prescribing in older people	• Implicit: knowledge-dependent, time-consuming and does not assess underprescribing • Explicit: time-consuming unless process is automated and the patient's perspective is often not taken into consideration
Computerized decision support systems	• Have the potential to alert the prescribing physician to drug-prescribing issues	• Existing systems are not geriatric specific; insufficient evidence for improvement in patient outcomes; high volume of alerts: risk of unimportant warnings
Geriatric medical services interventions	• Integrated care and detailed geriatric assessment can reduce length of hospital stay and the number of readmissions	• Pharmacotherapy must be part of the initial geriatric assessment for approach to work well • Heterogeneity in terms of structural components and care processes

generated to address any issues [29]. Finally, the pharmacist discusses with the patient how the medications are best taken and the medication scheduled can be implemented into the patient's daily life.

Authors of a recent literature review concluded, that in general, pharmacotherapy for older patients improved when pharmacists played a proactive role in performing medication reviews and were involved in the active education of other healthcare professionals. Nevertheless, a specific positive impact of pharmacists' interventions on health outcomes, quality of life or cost-effectiveness could not always be established [30]. Illustrative of this point is a randomized clinical trial (RCT) investigating pharmacist-assisted medication reconciliation, inpatient

pharmacist counselling, low-literacy adherence aids, and individualized telephone follow-up after hospital discharge. In the trial population of 851 adults hospitalized for acute coronary syndromes or acute heart failure the per-patient number of clinically important medication errors (incidence rate ratio, 0.92) or adverse drug events (incidence rate ratio, 1.09) was not significantly different between the intervention and control groups [31]. The primary reason that the trial failed to demonstrate any significant effects could be seen in a lack of integration between the pharmacists and other professional caregivers which is critical and was not insufficiently addressed in the study. This was confirmed by Spinewine et al. [30] who noted that results of pharmacist-driven interventions tend to show better results when pharmacists are skilled and work as part of a multidisciplinary team composed of physicians, nurses and other caregivers. For example, in the RCT conducted by Spinewine et al. [32] in which pharmaceutical care was delivered to hospitalized older patients by an experienced clinical pharmacist who worked contextually with the existing geriatric team, the results were superior in the intervention arm compared to the control arm. Specifically, intervention subjects experienced a significant improvement in the appropriateness of prescribing from hospital admission to discharge. In addition, when team-based care included pharmacists, meta-analysis demonstrated that a 47 % reduction in adverse drug events was possible [33].

These findings illustrate the complexity in globally assessing geriatric patients in regard to appropriate pharmacotherapy and judgment of ADRs. The research also suggests that isolated pharmacist-driven interventions are not likely to succeed; rather, team-based approaches in which pharmacists are fully appraised in the pharmacotherapy of older people are required. Finally, to better direct this kind of research, larger multicentre trials are needed as sample sizes of available RCTs are small [34–37].

Educational Interventions

Educational interventions of healthcare professionals vary broadly ranging from teaching, interactive workshops, and face-to-face interactions to providing decision algorithms. A systematic review of such interventions found mixed results [38] and especially singled out limitations of several studies as they did not define what data would be required to assess adequacy for a given level of intervention nor sample size calculations to determine acceptable type I and type II errors. Another review also suggested that mere dissemination of guidelines is unlikely to be effective, whereas active educational interventions in the form of workshops, meetings, and regular reports could improve drug treatment [39]. Taking together the results of the studies clearly imply that ongoing individualized, interactive, multidisciplinary, and multifaceted educational programs are a critical and important intervention to

succeed in increasing awareness of healthcare professionals in regard to prescribing medication in older patients.

Instruments to Detect Inappropriate Prescribing in Older People

Several tools are available to clinicians to assess whether medication is appropriate for older and multimorbid patients. These tools are either implicit, judgment-based, instruments that include clinical information available about the patient or explicit, criteria-based tools. The MAI is the most comprehensive and validated implicit tool available to date. The MAI is based on ten elements of drug prescribing: indication, effectiveness, dose, correct directions, practical directions, drug-drug interactions, drug-disease interactions, duplication, duration, and cost. Summation of the ratings produces a weighted score that is representative of whether prescribed drugs are appropriate whereby lower scores are indicative as being more appropriate [40]. While straightforward, calculating the MAI score is time-consuming and does not assess underprescribing. A study using adapted MAI scores found considerable utility in detection of drug-related problems in geriatric inpatients and was reliable with a low inter-rater variability as well as positive correlation between high score and drug-related hospital admission [41].

Explicit tools, on the other hand, are consensus-based standards focusing on drugs and diseases and include lists of drugs to avoid in general or lists combining drugs with clinical data. Although many explicit tools have been developed over the years [42–52], only the Beers criteria [53, 54] and Screening Tool of Older Persons' Prescriptions (STOPP) [55, 56] criteria have been examined in terms of their predictive validity.

Almost 25 years ago, Beers and his coresearchers set about developing a list of criteria using the Delphi approach that would lower the risk of drug prescribing in older persons [53]. The Beers criteria have since undergone several updates, with the latest revision in published in 2012 by the American Geriatrics Society using an evidence-based approach that identifies 53 drugs or drug classes divided into three categories: potentially inappropriate drugs to avoid independent of comorbidities; potentially inappropriate drugs to avoid in older adults with certain diseases and syndromes because they might cause exacerbation, and medications to be used with caution [54]. Based on the most recent criteria and using a community-dwelling sample of U.S. older adults (N = 18,475). Davidoff et al. [57] estimated that the potentially inappropriate medication (PIM) prevalence rate in the USA declined from 45.5 % in 2006–2007 to 40.8 % in 2009–2010. While this is an encouraging trend in the USA there is evidence that such criteria cannot be so easily applied in European countries; for example, several drugs listed in the 2003 Beers criteria were rarely prescribed or were not available in Europe and 2003 Beers-listed PIMs were not associated with ADRs in some studies [58].

Alternative tools initiated in 2008 and updated in 2015 termed STOPP (Screening Tool of Older Person's Prescription) and START (Screening Tool to Alert doctors to Right—appropriate, indicated—Treatment), include potentially inappropriate drugs (STOPP) as well as screening for omissions of indicated, potentially beneficial drugs (START) [55, 56]. The authors took a different approach by organizing criteria according to physiological systems and include both potentially inappropriate prescribing, and omission of potentially beneficial pharmacotherapy, which is missing from the Beers criteria. These START and STOPP criteria have now been endorsed by the European Union Geriatric Medicine Society (EUGMS). Perhaps what is most interesting about this approach is that their application leads to significant and durable improvements in the appropriateness of prescribing at discharge and for *up to 6 months after discharge*, indicating that this is a pragmatic tool capable of producing long-lasting, beneficial effects for older people [59, 60]. As an example of validation, a prospective study conducted involving 600 consecutive inpatients aged 65 or more utilizing STOPP criteria demonstrated an association with avoidable adverse drug events that cause or contribute to urgent hospitalization, a result that could not be shown with the Beers criteria [61].

Computerized Decision Support Systems

Another method to detect inappropriate drug prescribing and drug interactions and reduce the risk of iatrogenic drug problems has been the 'intelligent' computerized decision support system (CDSS). This is basically a series of algorithms implemented through the use of specially designed software. Such algorithms are generally rule based. For example, based on known data about drugs in geriatric populations upon a physician entry of a prescription order the software will check whether the drug dosage is appropriate and whether it is contraindicated given the patient's comorbidities. Although the CDSS has the potential to alert the prescribing physician to drug-prescribing issues, a recent review article concluded that improvements in patient outcomes have not yet need established [62]. Part of the reason for this is that physicians usually have the ability to override the system. When a 'hard stop' is employed in conjunctions with computerize order entry this could lead to a more effective system but could also delay critical patient medications [63]. Performance issues depend on how specific the information in the system is as well as the system is by itself considering that if the system does not recognize a geriatric patient, or impairments in individuals—for example, cognitive deficits—it will be of little use in older people as a means of stopping inappropriate drug prescribing.

Geriatric Medical Services Interventions

The use of multidisciplinary teams in medicine always confers advantages over non-integrated healthcare providers within any system, and geriatrics is no exception. When the medical and physiological complexity of older patients is considered by the team prior to any pharmacotherapy, the risk of an ADR can be lessened. Ideally, integrated medicine management is delivered starting with hospital admission and following up after discharge in a manner that is transparent to the patient with continuous information flow between hospital physicians and nurses, clinical pharmacists inside or outside the hospital, and primary care physicians. An ultimate patient benefit is that this process leads to optimized drug therapy with reduced length of hospital stay, longer time to readmission, and decreases the number of readmissions [64].

The traditional medical approach to treatment of older patients, even within a multidisciplinary framework, is not always enough to fully assess all problematic areas. Therefore, a more comprehensive geriatric assessment may be required to improve the pharmacotherapy and reduce the ADR rate. When this is done via the production of an individual care plan tailored to an older person that includes a more thorough evaluation it will result in enhanced care planning and better quality of care [65]. In this process, the issue of pharmacotherapy is not seen as a separate issue, but as part of the overall treatment plan, embracing a more holistic program in which drug prescribing is one avenue of treatment that is integrated into others. One further benefit is that the drug prescription plan may be simplified based on pharmacological and healthcare needs of the individual patient with concurrent reductions in drug-related adverse events and increases in the quality of drug prescribing [66–69]. In a large study employing a randomized 2×2 factorial controlled design utilizing patients in 11 Veterans Affairs (VA) hospitals, inpatient geriatric unit and outpatient geriatric clinic teams evaluated and managed patients according to published guidelines and VA standards in the intervention arms [70]. A 35 % reduction in the risk of serious ADRs compared with usual care was observed in outpatient geriatric clinic care and inpatient geriatric unit care with a significant reduction of unnecessary and inappropriate drug use and underuse. Moreover, outpatient geriatric clinic care reduced the number of clinical conditions that were caused by the omission of drugs significantly.

In the context of comprehensive geriatric assessment, the CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) project generated 19 recommendations relating specifically to five chronic conditions commonly experienced in older persons: diabetes, hypertension, congestive heart failure, atrial fibrillation and coronary heart disease. The intent of the project was to make healthcare providers more aware that goals of treating older people in respect of pharmacotherapy may be different from younger persons due to patient related factors and the presence of conditions routinely experienced by this patient population, such as limited life expectancy, functional and cognitive impairment and

geriatric syndromes. These conditions frequently limit drug benefits or can cause negative outcomes in respect of drugs and need to be considered when prescribing to such patients [71].

Conclusion

Single interventions as described in this review rarely achieve significant enhanced patient outcomes by themselves, but are far more effective when bundled together in a rational and integrated fashion—for instance, the effectiveness of a medication review by including a pharmacist in the context of a multidisciplinary team. Approaching the subject of complex clinical and therapeutic problems of geriatric patients with a global review that includes assessing each patient's clinical and functional parameters before tackling the pharmacological issues is likely to succeed better than merely reviewing pharmacotherapy by itself. If future clinical research focuses on better integration of all methods with demonstrated improvements in patient outcomes, more healthcare providers are likely to see the benefits of such approaches and adopt them.

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